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For Educational Services & Training

Ramadan & Medications

Presented by:

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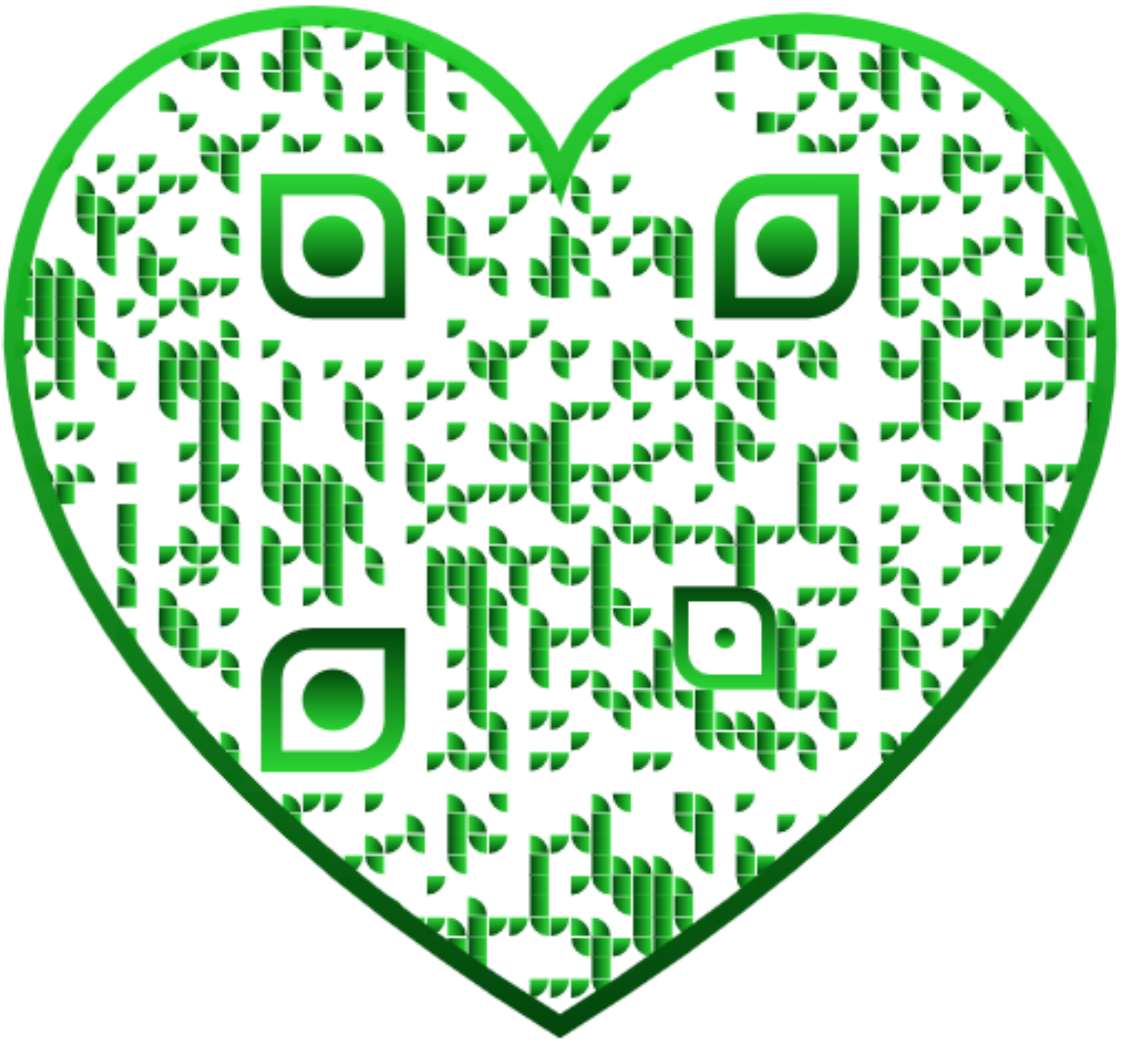
MSc, PhD, Clinical Pharmacy & Pharmacy Practice



Objectives

1. To know which **route of administration** that could BREAK the fast

2. To know **how medications** could be **managed** in Ramadan

3. To know how to **optimize diabetic medications** in Ramadan

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Outline

- Overview
- Route of administration and fasting
- Dosing schedule and fasting
- Diabetics medications management

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Overview

- Ramadan is the ninth month of the Islamic lunar calendar

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Overview

- Ramadan can occur in **any of the four seasons**

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Overview

- The hours spent fasting vary accordingly from 11- 18 hours a day

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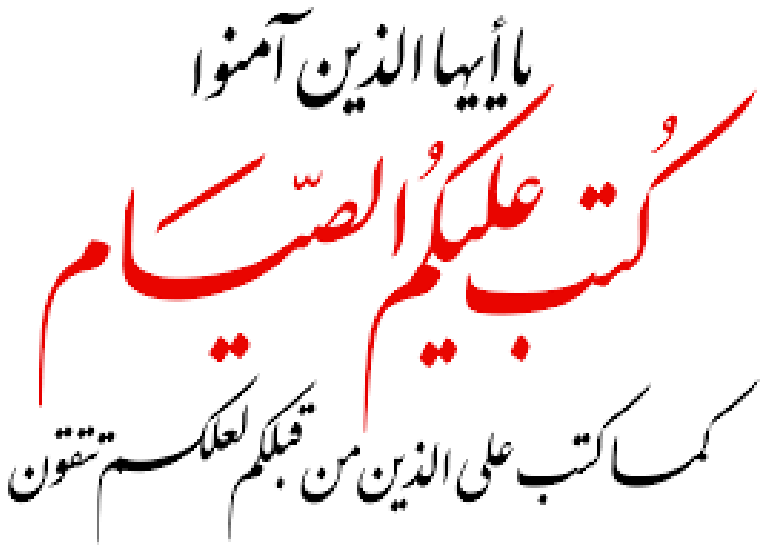
Overview

- Adult Muslims are Required to Fast



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Overview

- Adult Muslims are **must abstain** from

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Overview

- Fasting in **other religions**

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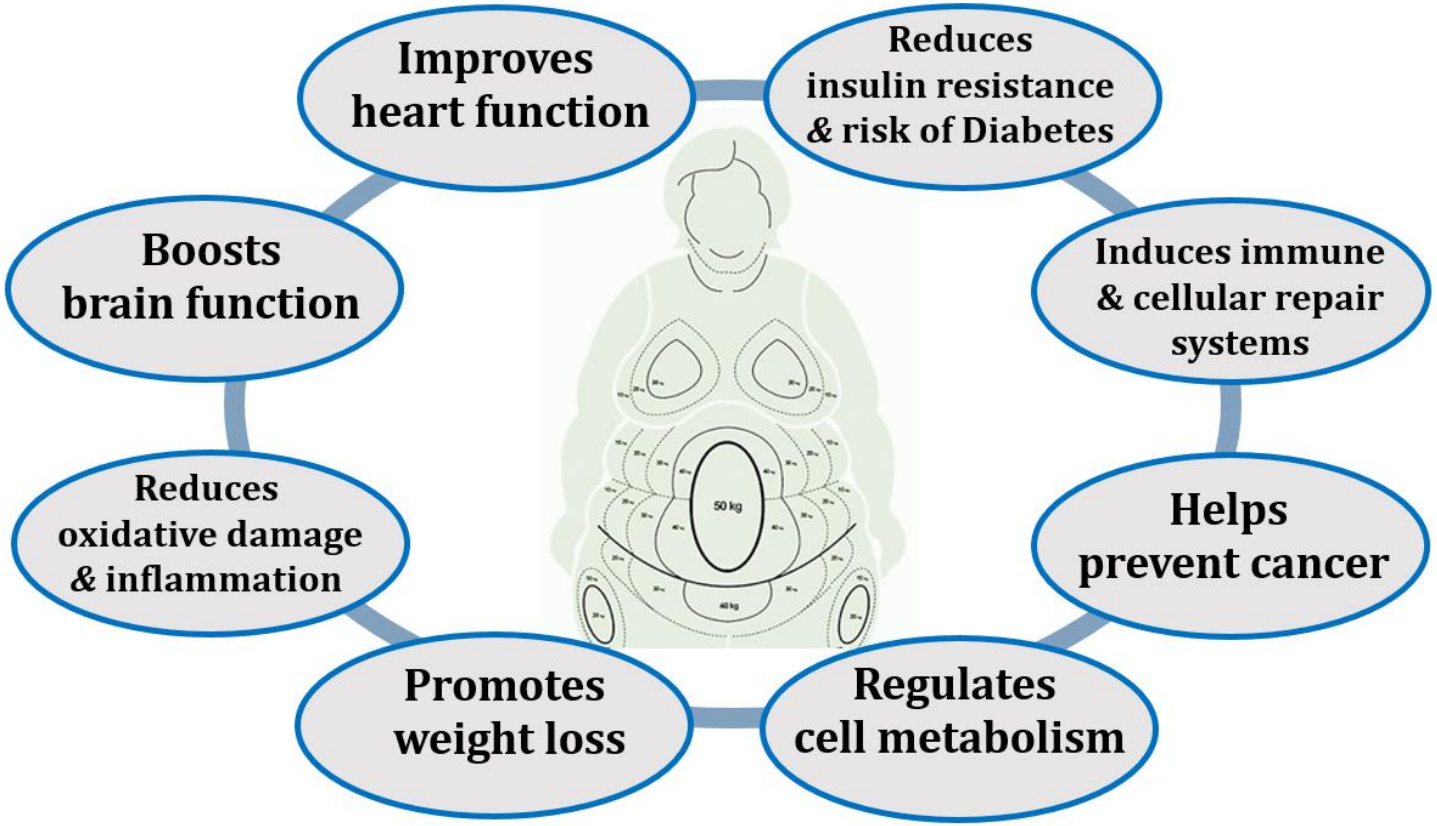
Overview

- Fasting effect



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Ferah Armutcu, Fasting may be an alternative treatment method recommended by physicians. (Electron J Gen Med 2019)

In Ramadan

- Rhythms of life and habits are changed during Ramadan

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In Ramadan

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In Ramadan

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In Ramadan

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Physiological and pharmacokinetic changes

- Drug absorption can be affected
  - During fasting, **the gastric pH significantly decreases up to 1**

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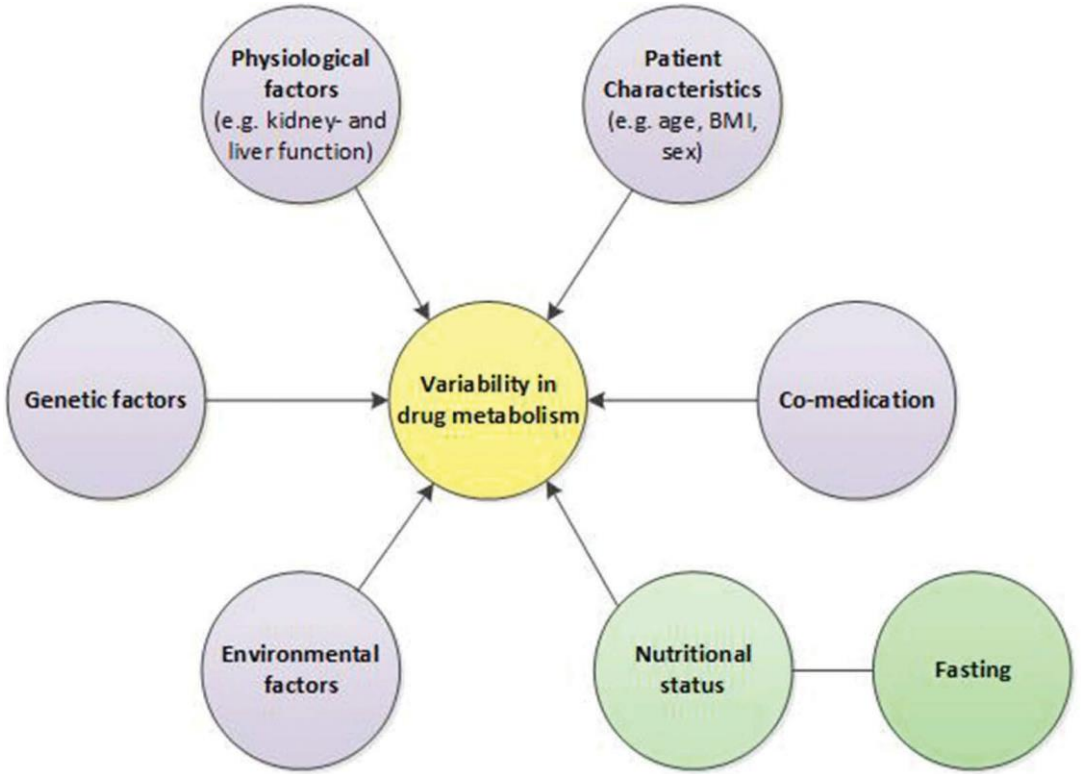
Physiological and pharmacokinetic changes

- Fasting **is part of a complex interplay** of factors affecting drug response



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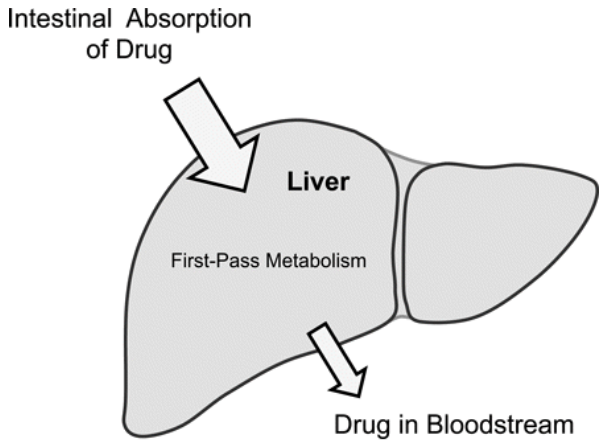
Laureen A. Lammers et al.Romijn (2020) The effects of fasting on drug metabolism, Expert Opinion on Drug Metabolism & Toxicology, 16:1, 79-85,

Physiological and pharmacokinetic changes

- Drug metabolism can be altered (**increased/decreased**)
  - Alteration **CYP450-mediated** drug metabolism (more studies are needed)



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Physiological and pharmacokinetic changes

- Effects of **short-term fasting (36 hours)** on human drug metabolizing enzymes

Human drug metabolizing enzyme	Enzyme activity *% increase (↑) or % decrease (↓) compared to control**
CYP1A2	↑ 17% ($p = 0.04$)
CYP2C9	↓ 19% ($p < 0.01$)
CYP2C19	*No effect*
CYP2D6	↑ 13% ($p < 0.01$)
CYP3A4	↑ 12% ($p < 0.01$)
UGT1A4/2B4/2B7	↓ 13% – 20% ($p < 0.01$)

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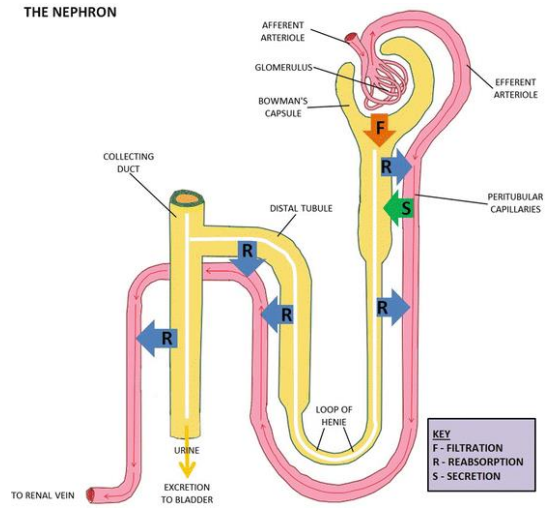
Laureen A. Lammers et al.Romijn (2020) The effects of fasting on drug metabolism, Expert Opinion on Drug Metabolism & Toxicology, 16:1, 79-85,

Physiological and pharmacokinetic changes

- Drug execration **might be decreased** in CKD
  - These patients are **more likely** to have adverse outcomes



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Drug regimens in Ramadan

- Drug regimens during the fasting period of Ramadan are changed

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Drug regimens in Ramadan

- Patients **arbitrarily change** their drug regimen **WITHOUT SEEKING MEDICAL ADVICE**, e.g. they:
  - **STOP** their medications
  - **MODIFY** the timing of administration/intake
  - **CHANGE** the frequency
  - **CHANGE** the total daily dosage

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Drug regimens in Ramadan

- Aslam et al: (surveyed 81 patients)
  - 58% changed
- Another survey of 325 outpatients in a Kuwaiti hospital
  - 64% changed

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Aslam M, Healy MA. Compliance and drug therapy in fasting Moslem patients. *J Clin Hosp Pharm 1986;11:321-5.*

Aslam M, Assad A. Drug regimens and fasting during Ramadan: a survey in Kuwait. *Public Health 1986;100:49-53.*

Drug regimens in Ramadan

- Healthcare are responsible to provide information to patients regarding their drugs in Ramadan

1. Route of administration
2. The rhythm and schedule of administration

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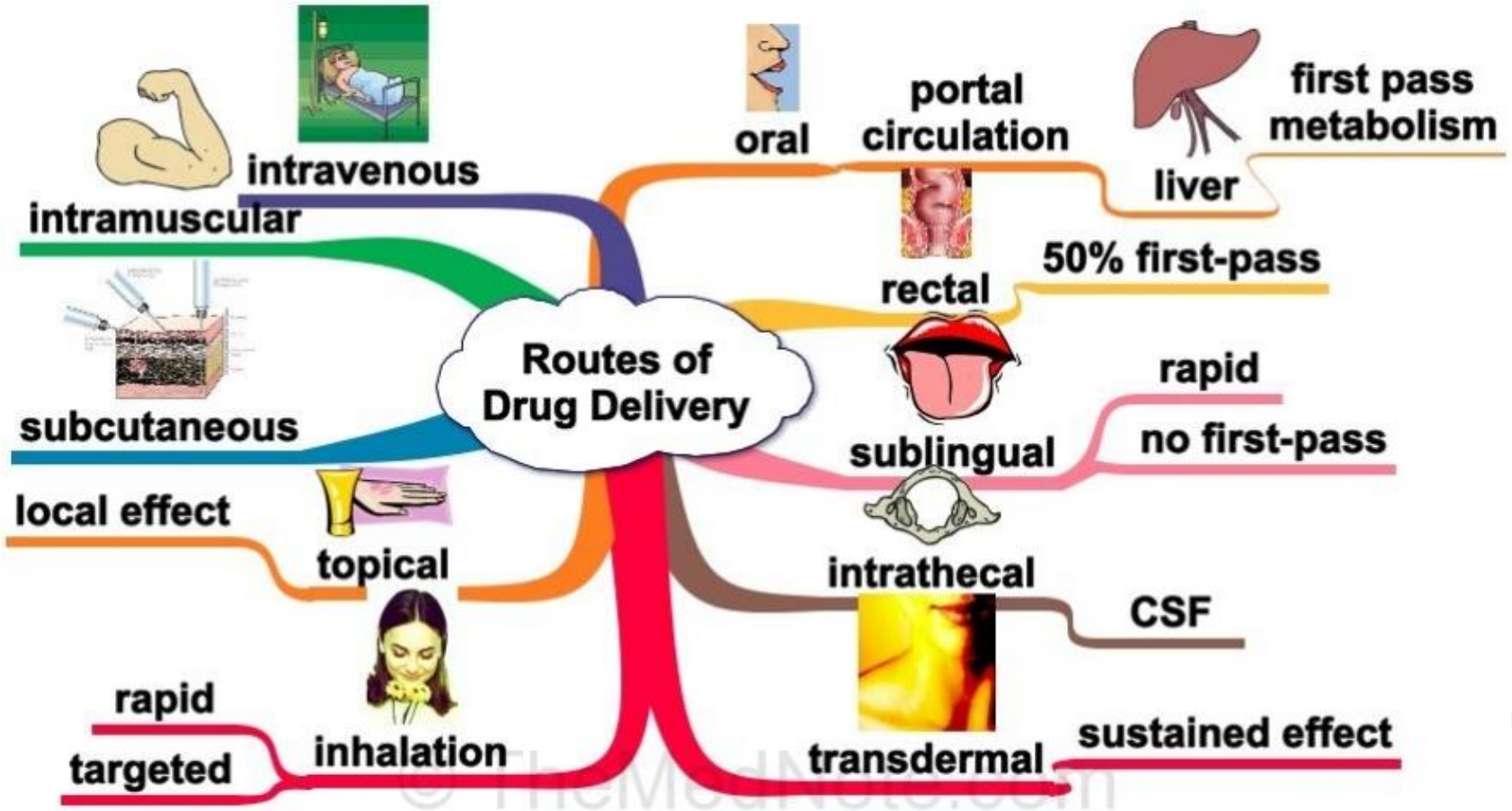
Route of administration & Fasting



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Rules

- Anything goes through the **mouth and reaches the stomach** will BREAK the fast

- Anything considered as food or drinks will BREAK the fast

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Oral Medication

- **Therefore,** any oral medication that reached the stomach will BREAK the fast

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What about others ???

- Notice
  - Here, I'll mention the opinion of :

1. Assemblies of Islamic Jurisprudence (Fiqh),1997, Jeddah
2. Religious-medical seminar held in Morocco in June 1997
3. Some Islamic scholar

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Eye, Ear, and Nose drops, and Nasal Inhalers, provided **NOTHING** is swallowed into the stomach

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Nitroglycerin tablets placed under the tongue for the treatment of angina (provided **NOTHING** is swallowed into the stomach)

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Insertion into the vagina of pessaries, medical ovules, and vaginal washes

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Injections through the skin, muscle, joints, or veins, with the **EXCEPTION** of intravenous feeding

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Oxygen and anaesthetic gases

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - Mouthwash, gargle, or oral spray (provided **NOTHING** is swallowed into the stomach)

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- The following dose **NOT** Breaking Fasting
  - All substances absorbed into the body through the skin, such as creams, ointments, and medicated plasters

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Assemblies of Islamic Jurisprudence(Fiqh), 1997, Jeddah

- They **SOTP** in the following (needs more research):
  - Inhalers
  - Anal injections or suppositories

Religious-medical seminar held in Morocco in June 1997

- Their recommendations are **as the same as** (Assemblies of Islamic Jurisprudence (Fiqh)

- **Except:** (majority of them allowed the following)

  - Inhalers
  - Anal injections
  - Nose drops, nose sprays
  - Surgery involving general anaesthesia, if the patient decided to fast.

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Notice

- There are **difference opinion** in the following

1. Nasal sprays, and drops
2. Inhalers
3. Anal injections and suppositories
4. General anaesthesia

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Nasal sprays, and drops

- Nasal spry and drops **mostly Will Break** the Fast (best to avoiding it)

ثبت عن رسول الله صلى الله عليه وسلم أنه قال للقيط بن صبرة: ((أسبغ الوضوء وخلل بين الأصابع وبالغ في الاستنشاق إلا أن تكون صائماً)) رواه الترمـــذي

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Inhalers

- Are they reach the stomach or NOT?
  - Most likely (**NOT** reach the stomach)
  - So, inhalers **most likely** they will **NOT** Break the fast

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Others

- Anal injections or suppositories
  - they will **NOT** break the fast

- General anaesthesia (like COMA):
  - If some hours will **NOT** break the fast
  - If dawn to sunset **will BREAK** the fast

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Dosing schedule

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Dosing schedule

- Drug doses can be taken only **between sunset and dawn,** and the time span between them is **shorter than** outside Ramadan

- In Yemen (~ **13.5 hours**) (**Ramadan 1444 H**)

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Dosing schedule

- **In General**

1. **Single daily dose**

2. **Two or more daily doses**

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Single daily dose

- The **easiest situation** is that of patients who have a usual **evening dose**.
  - **BUT**
- When the usual intake is in the morning or during the day **the health care providers must be careful when delaying the intake to the evening**
  - **WHY?!!**

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Single daily dose

- **Because**

- The **efficacy and toxicity** of many drugs can vary depending on the time of administration in relation to the **circadian rhythms** of biochemical, physiological, and behavioural processes

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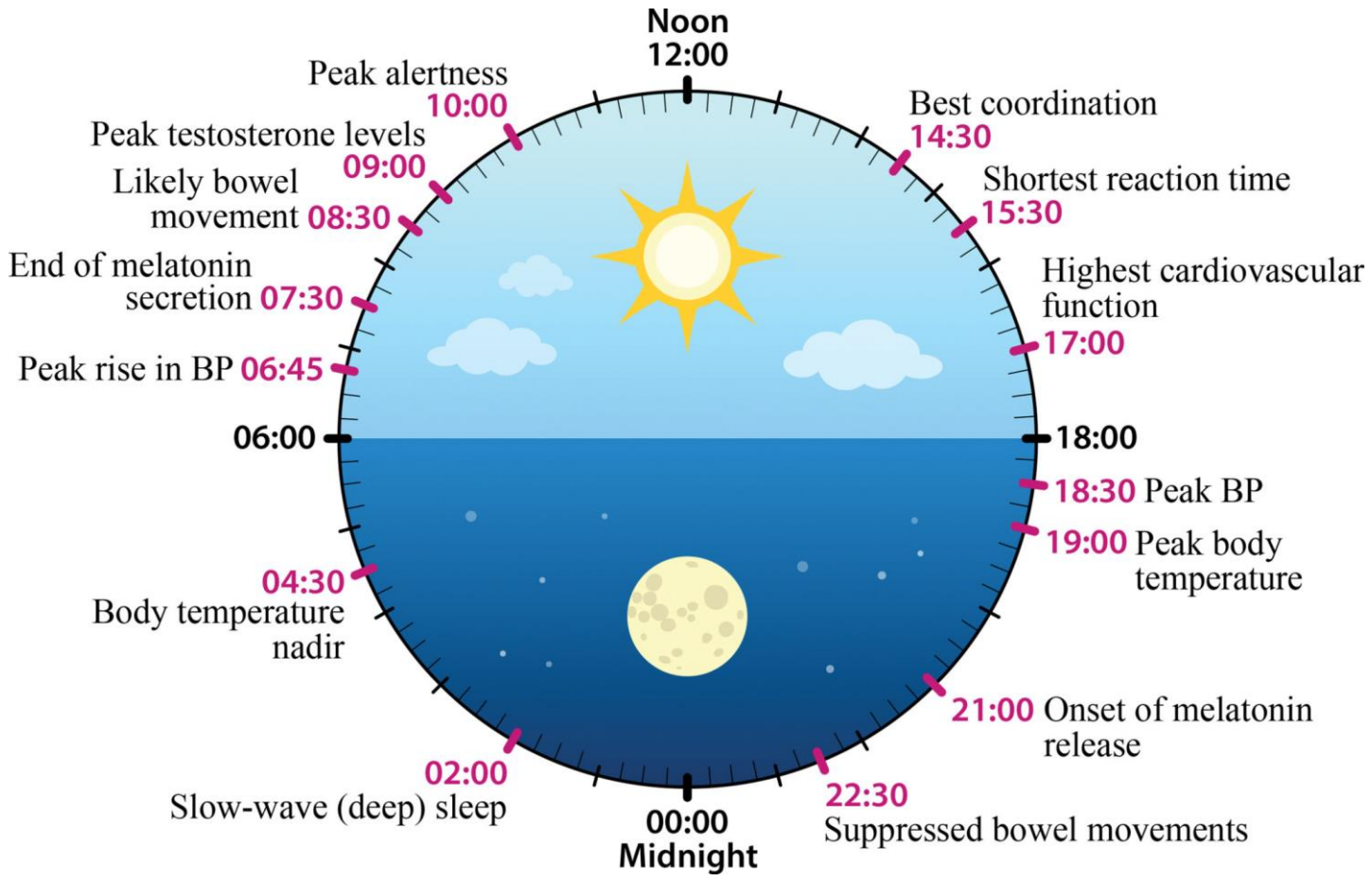
Physiological or biochemical functions are at peak



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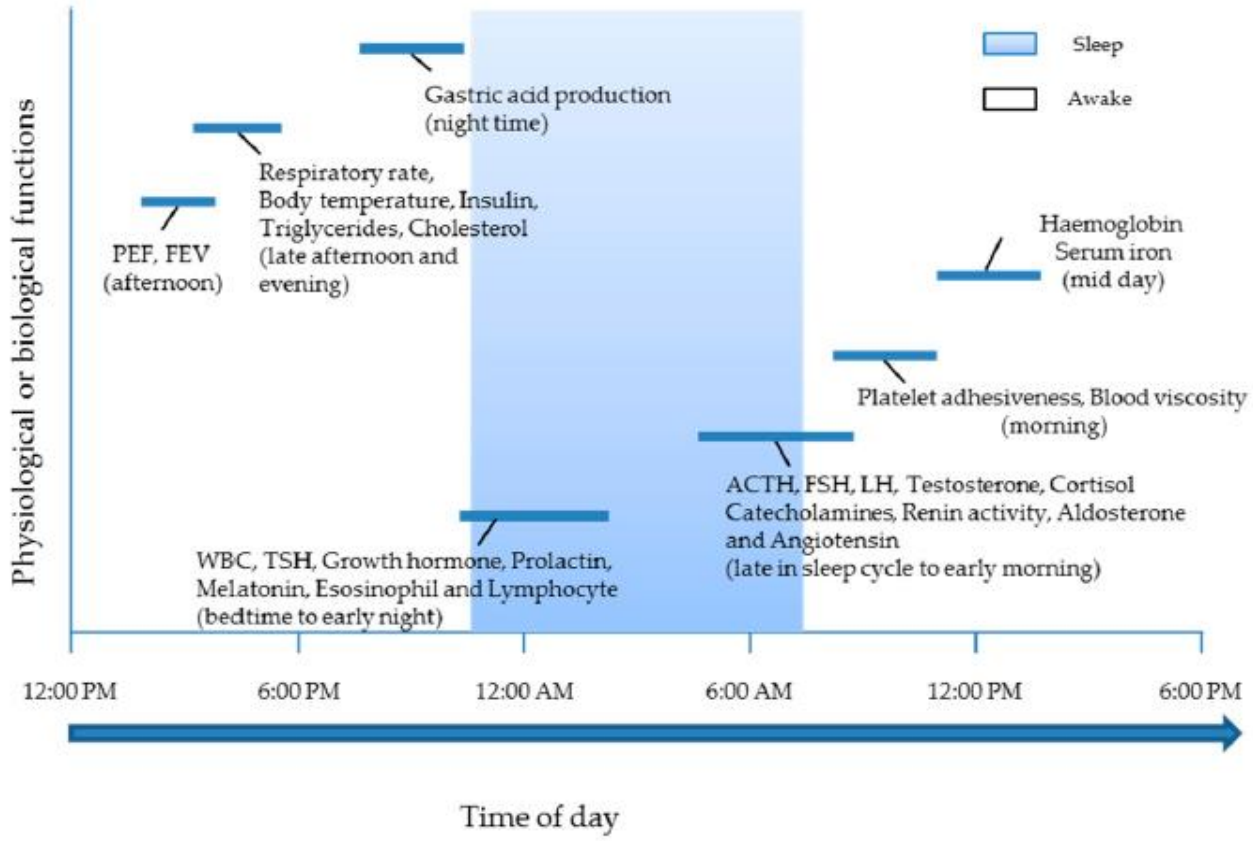
James C. Walton et al. Circadian Variation in Efficacy of Medications, Clin Pharmacol Ther. 2021 June ; 109(6): 1457–1488

Physiological or biochemical functions are at peak



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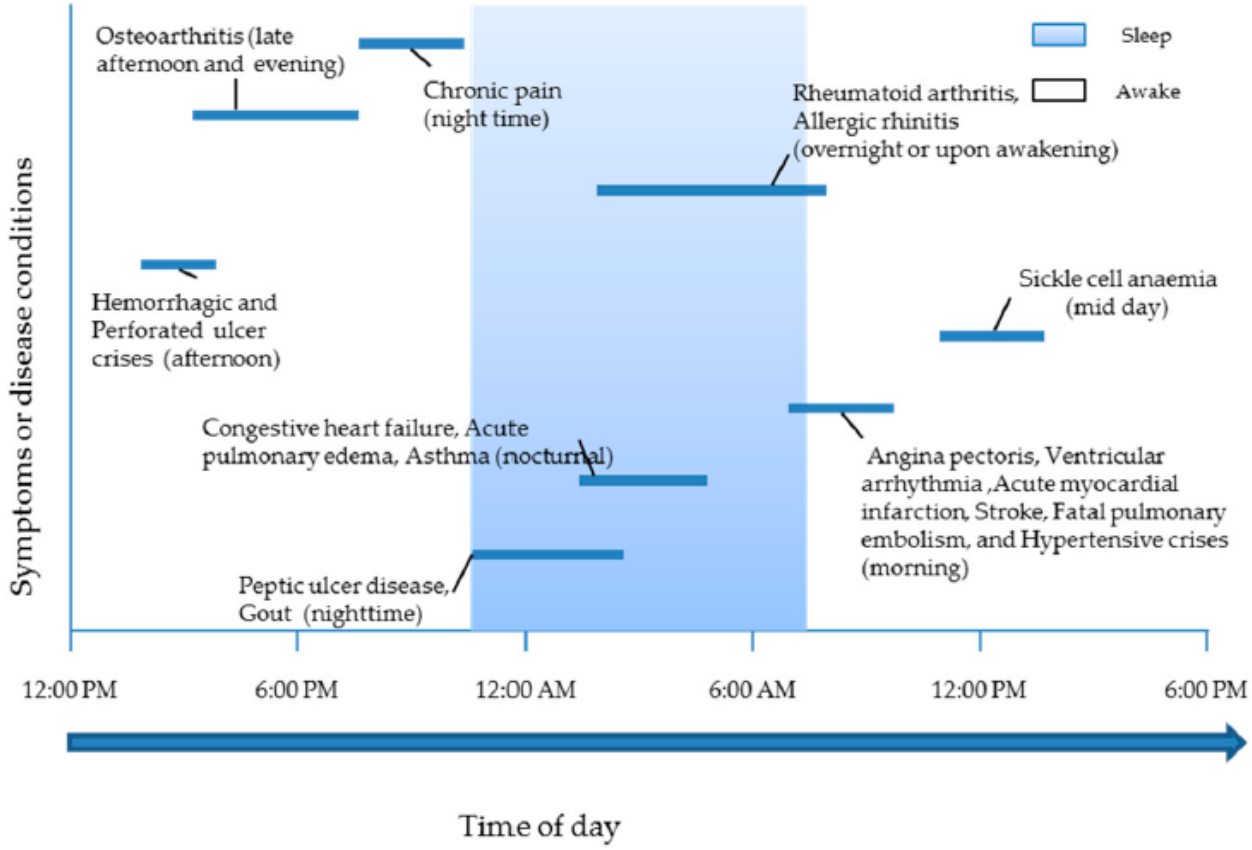
Gagandeep Kaur et al. Timing of Administration: For Commonly-Prescribed Medicines in Australia. Pharmaceutics 2016

Symptoms or events of diseases are more frequent


Osteoarthritis (late afternoon and evening)
Chronic pain (night time)
Rheumatoid arthritis, Allergic rhinitis (overnight or upon awakening)
Sleep
Awake
Hemorrhagic and Perforated ulcer crises (afternoon)
Sickle cell anaemia (mid day)
Congestive heart failure, Acute pulmonary edema, Asthma (nocturnal)
Angina pectoris, Ventricular arrhythmia ,Acute myocardial infarction, Stroke, Fatal pulmonary embolism, and Hypertensive crises (morning)
Peptic ulcer disease, Gout (nighttime)
Symptoms or disease conditions
12:00 PM
6:00 PM
12:00 AM
6:00 AM
12:00 PM
6:00 PM
Time of day

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Gagandeep Kaur et al. Timing of Administration: For Commonly-Prescribed Medicines in Australia. Pharmaceutics 2016

Chronotherapy

- The administration of medication or treatment **in coordination with the body's circadian rhythms** to maximize effectiveness and minimize side effects

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Chronotherapy

Drugs	Suggested time
Amlodipine	Morning
Diltiazem	Evening
Aspirin	Evening
Lisinopril	Evening
Ramipril	Morning
Nebivolol	Morning/ **Evening**
Valsartan	Evening
Candesartan	Evening
Diuretics (thiazides, torasemide)	Morning/**Evening**
Vildagliptin	Morning/**Evening**
Rivaroxaban	Evening
Vitamin D3	Evening
Calcium	Morning/ Evening

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James C. Walton et al. Circadian Variation in Efficacy of Medications, Clin Pharmacol Ther. 2021 June ; 109(6): 1457–1488
Shu-yi Zhou et al. Optimal Time to Administer Once-Daily Oral Cardiovascular Agents: Evidence Based on Randomized Clinical Trials in the Last Ten Years. J Geriatr Med Gerontol 2018

Chronotherapy

- **Limitations**

1. **Small** Studies

2. **Conflicting** results

3. Did **not take** into account variations in the **sleep-wake routines** of participants

4. **Not** conducting in **Ramadan**

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Two or more daily doses

- During Ramadan:
- Accurate distribution of drugs (**Difficult**)
- **Usually:**
  - One at the break of fasting (**Iftar**)
  - Second one before the beginning of fasting (**Suhoor**)

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Two or more daily doses

- **These alterations could:**

1. Affect the drug's plasma concentration profile

2. Therefore, its efficacy and tolerance

   (esp. **narrow therapeutic index drugs**)

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Theophylline and Fasting

- Study done in 12 stable asthma patients take it twice daily
  - (**8 out 12 had S/Es**) in Ramadan
  - (**4 out 12 has S/Es**) outside Ramadan
- Fasting Affecting Theophylline

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Daghfous J, Beji M, Louzir B, Loueslati H, Lakhal M, Belkahia C. Fasting in Ramadan, the asthmatics and sustained release theophylline. *Ann Saudi Med 1994;14:523*

The Solution ??

- Using **slow release** formulations
- Using a drug with a **longer elimination** half life

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Slow Release Formulations

Immediate Release	Slow Release
Metoprolol	Metoprolol XR
Valproic acid	Valproic acid CR
Carbamazipine	Carbamzipine (600 mg retard)
Levetiracetam	Levetiracetam (500 mg XR)
Diclofenac (50 mg)	Dicloofenac retard (100mg)
Ketoprofen (100 mg)	Ketoprofen SR (150 mg)

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Long Acting Drugs

Short Acting	Long Acting
Captopril	Lisinopril
Ibuprofen	Piroxicam
Clarithromycin	Azithromycin
Ciprofloxacin	Levofloxacin / Moxifloxacin
Metronidazole	Tinidazole
	Cefixime

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Oral anticoagulants

Short acting	Long acting
Dabigatran*	Rivaroxaban
Apixaban*	

***Note:**

Take after full Iftar and Suhoor

Interval should be ≥ 8 hours

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Your Guide to a Better Future

دليلك لمستقبل أفضل

Diabetic medications

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Diabetic medications

- Most people with **type 2 diabetes** can fast safely with appropriate medical advice and management before and during fasting.

- However, people with **type 1 diabetes** need special attention.

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Diabetic medications

- The main concern for diabetes management during Ramadan is **hypoglycemia.**

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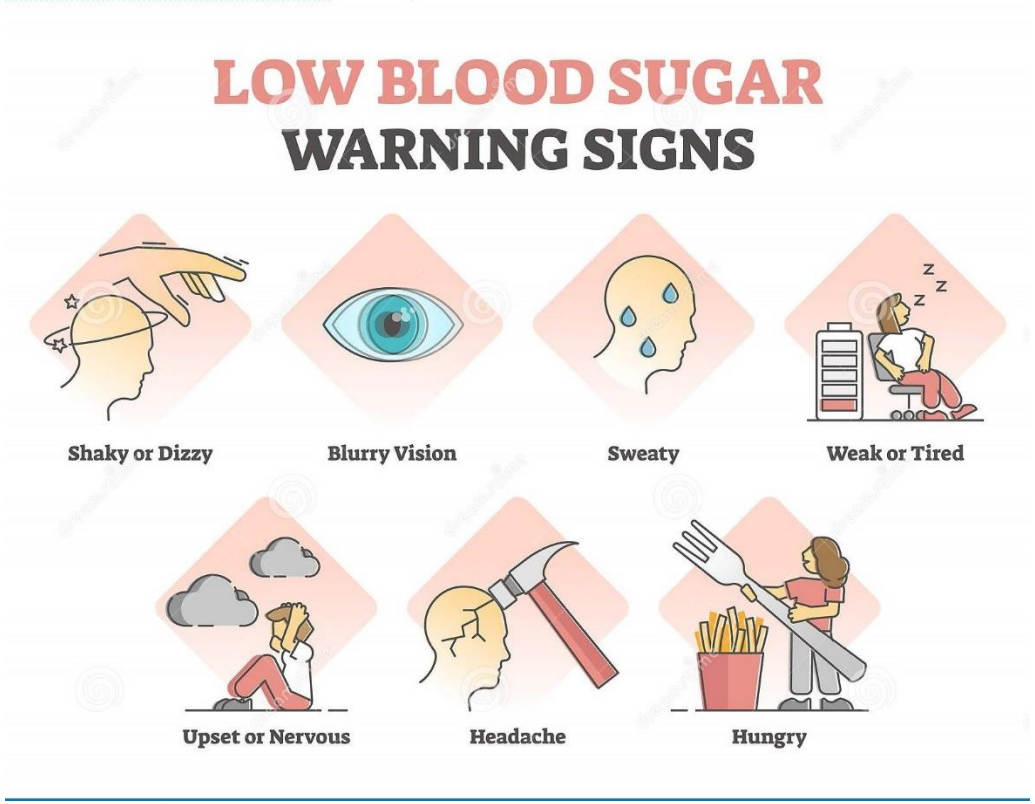
Diabetic medications

- **Hypoglycemia symptoms** (Patient awareness)



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Diabetic medications

- Very high risk (**People with any of the following**)
  - Severe or **recurrent episodes of hypoglycemia** in the **three months before** Ramadan
  - History of **hypoglycemic unawareness**
  - **Poor glycemic control** before the month of Ramadan
  - **Acute illness**
  - **Poorly** controlled **type 1 diabetes**
  - **Comorbidities** such as chronic kidney disease

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Diabetes type and duration	
Type 1 diabetes	1
Type 2 diabetes	0
Duration of diabetes	
Duration ≥ 10 years	1
Duration < 10 years	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
History of hypoglycemia and hypoglycemia unawareness	
Hypoglycemia unawareness	6.5
Recent severe hypoglycemia	5.5
Recurrent hypoglycemia	3.5
Hypoglycemia < once a week	1
No hypoglycemia	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Glycemic control	
A1c > 9%	2
A1c 7.5–9%	1
A1c < 7.5%	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Type of Treatment	
Multiple daily premixed insulin regimen	3
Basal bolus regimen/Insulin pump	2.5
Once daily premixed insulin	2
Basal insulin only	1.5
Older generation sulfonylureas (Glibenclamide)	1
Second generation sulfonylureas(SU) or Repaglinide	0.5
Non-insulin and non-SU agents	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Self-monitoring of blood glucose(SMBG)	
No adequate SMBG checks	2
Suboptimal SMBG checks	1
Adequate SMBG checks	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Occurrence of Diabetic ketoacidosis/ Hyperglycemic hyperosmolar state	
In last 3 months	3
In the last 6 month	2
In the last 12 months	1
None	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Cardiovascular complications/co-morbidities	
Unstable	6.5
Stable	2
None	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Renal complications/co-morbidities	
GFR < 30 mL/min/Stage 4 CKD	6.5
GFR 30–44 mL/min/Stage 3b CKD	4
GFR 45–59 mL/min/Stage 3a CKD	2
GFR ≥ 60 mL/min	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Pregnancy	
Blood glucose not within target range	6.5
Blood glucose within target range	3.5
Not pregnant	0
Frailty and cognitive function	
Impaired cognition or Frail	6.5
>70 year without home support	3.5
None	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Risk Factors	Score
Physical labor	
High intense	4
Moderate intense	2
None	0
Prior Ramadan experience	
Negative experience	1
No particular experience	0
Fasting hours based on location	
≥16 h	1
<16 h	0

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IDF-DAR 2021 risk factors and scores for risk stratification

Interpretation	
Score 0–3 (Low risk)	Should be able to fast
Score 3.5–6 (Moderate risk)	Advised not to fast
Score > 6 (High risk)	Should not fast

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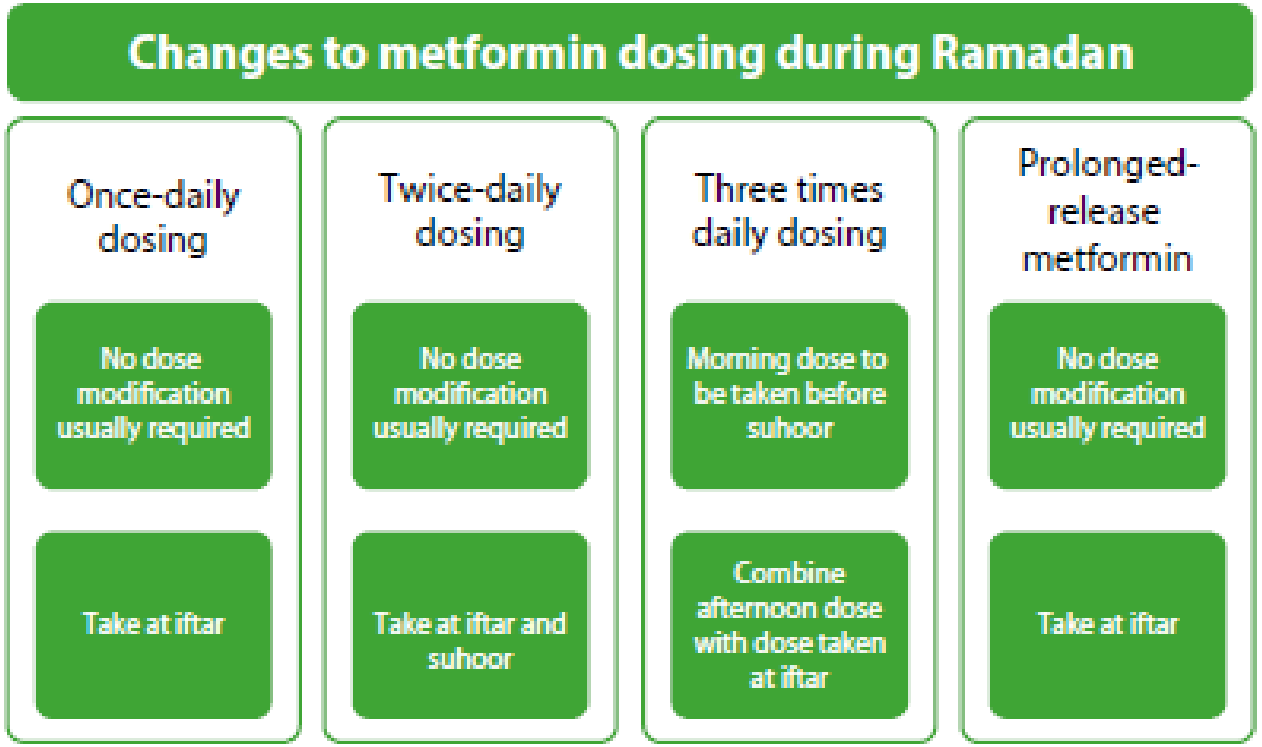
Diabetic medications

- **Metformin**


Changes to metformin dosing during Ramadan
Once-daily dosing
No dose modification usually required
Take at iftar
Twice-daily dosing
No dose modification usually required
Take at iftar and suhoor
Three times daily dosing
Morning dose to be taken before suhoor
Combine afternoon dose with dose taken at iftar
Prolonged-release metformin
No dose modification usually required
Take at iftar

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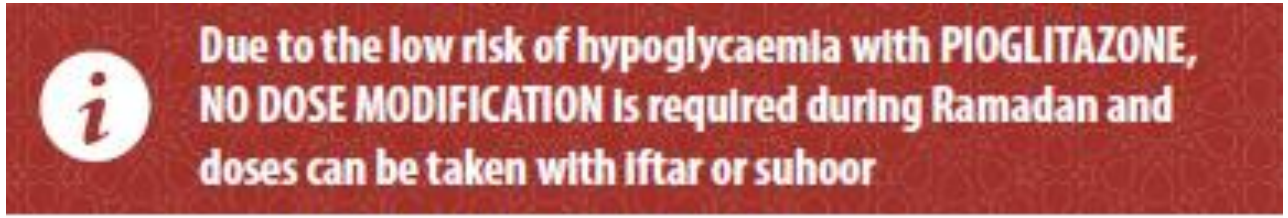
Diabetic medications

- **Thiazolidinediones**


Due to the low risk of hypoglycaemia with PIOGLITAZONE, NO DOSE MODIFICATION is required during Ramadan and doses can be taken with iftar or suhoor

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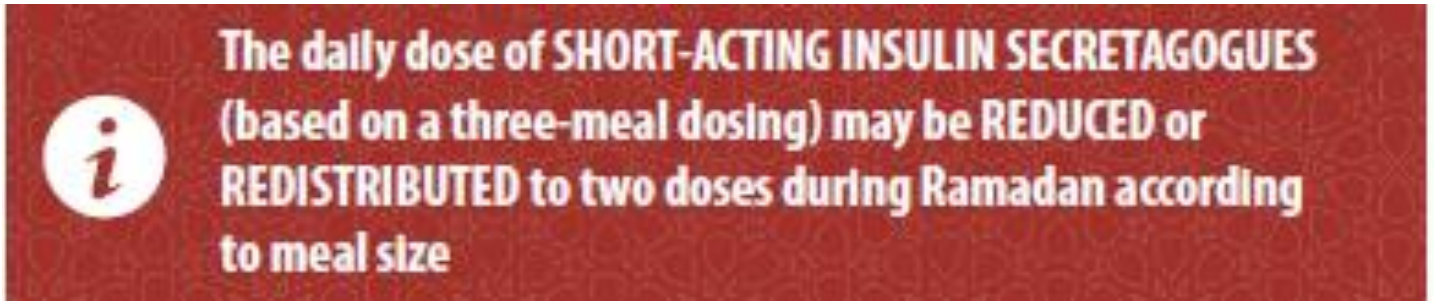
Diabetic medications

- **Short-acting insulin secretagogues (e.g. repaglinide)**


The daily dose of SHORT-ACTING INSULIN SECRETAGOGUES (based on a three-meal dosing) may be REDUCED or REDISTRIBUTED to two doses during Ramadan according to meal size

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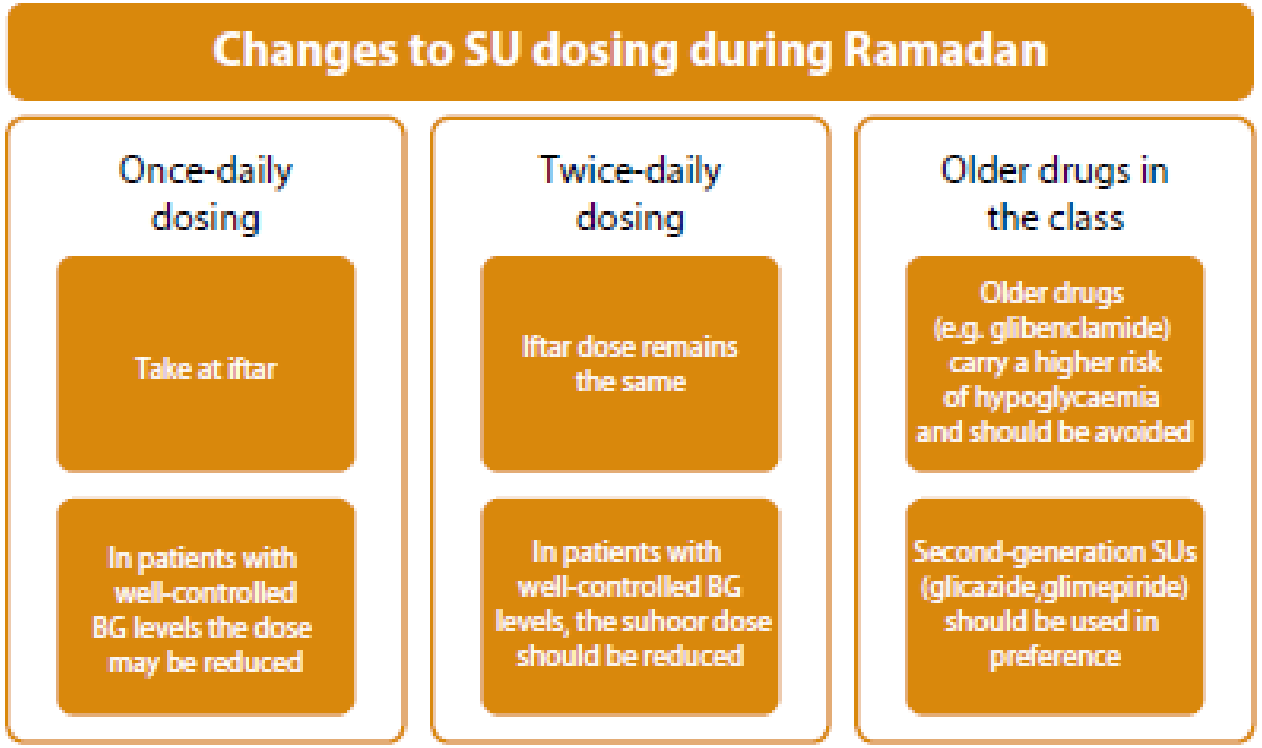
Diabetic medications

- **Sulphonylureas (SU)**


Changes to SU dosing during Ramadan
Once-daily dosing
Take at iftar
In patients with well-controlled BG levels the dose may be reduced
Twice-daily dosing
Iftar dose remains the same
In patients with well-controlled BG levels, the suhoor dose should be reduced
Older drugs in the class
Older drugs (e.g. glibenclamide) carry a higher risk of hypoglycaemia and should be avoided
Second-generation SUs (glicazide,glimepiride) should be used in preference

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Diabetic medications

- **Sodium-glucose co-transporter-2 (SGLT2) inhibitors (e.g. dapagliflozin)**

SGLT2 inhibitors can be used with CAUTION in SOME patients. During Ramadan NO DOSE ADJUSTMENT is required and it is advised that the dose be taken with iftar

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Diabetic medications

- **Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. sitagliptin)**

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Diabetic medications

- **Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) (e.g. Exenatide)**

As long as GLP-1 RAs have been appropriately DOSE-TITRATED prior to Ramadan (6 weeks before), NO FURTHER TREATMENT MODIFICATIONS are required

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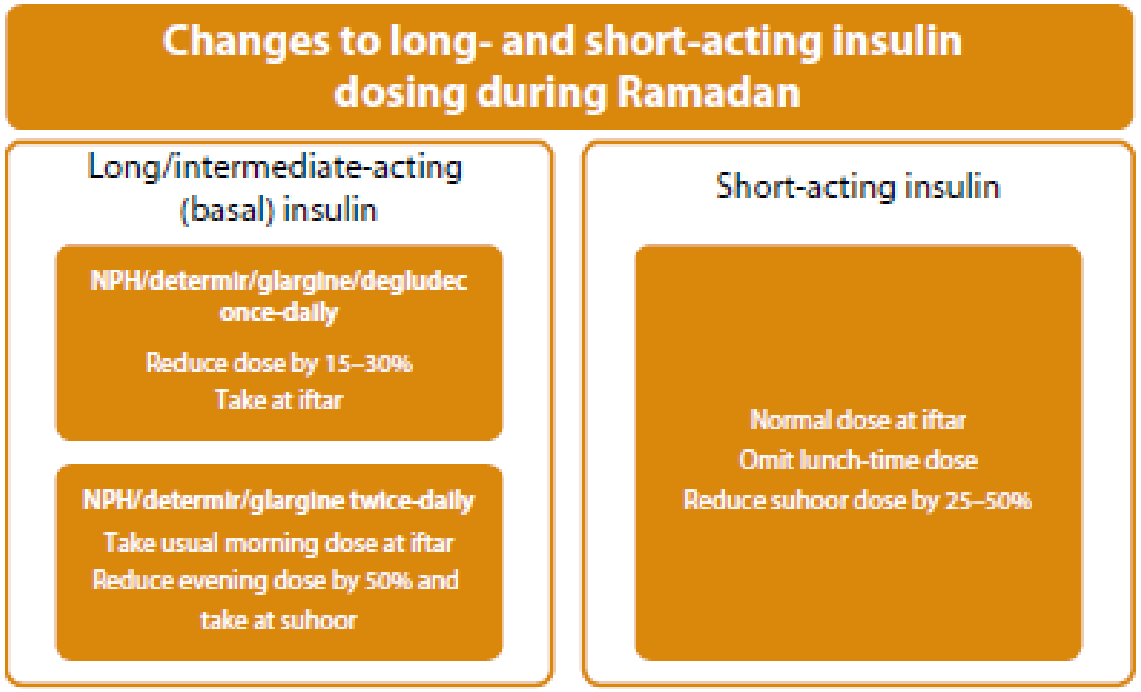
Diabetic medications

- **Insulin**


Changes to long- and short-acting insulin dosing during Ramadan
Long/intermediate-acting (basal) insulin
NPH/determir/glargine/degludec once-daily
Reduce dose by 15–30%
Take at iftar
NPH/determir/glargine twice-daily
Take usual morning dose at iftar
Reduce evening dose by 50% and take at suhoor
Short-acting insulin
Normal dose at iftar
Omit lunch-time dose
Reduce suhoor dose by 25–50%

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Diabetic medications

- **Insulin**

Type of Insulin	Dosing Frequency	Recommended Change
Basal insulin (insulin glargine/NPH/Degludec/Detemir)	Once daily	Reduce dose by 15–30% and Take at Iftar (sunset meal)
Basal insulin (insulin glargine/NPH/Degludec/Detemir)	Twice daily	Take usual morning dose at Iftar (sunset meal), Reduce evening dose by 50% and Take at Suhoor (pre-dawn meal)
Short-acting insulin/Bolus insulin		Take normal dose at Iftar (sunset meal), Skip lunch time dose and Reduce Suhoor (pre-dawn meal) dose by 25–50%

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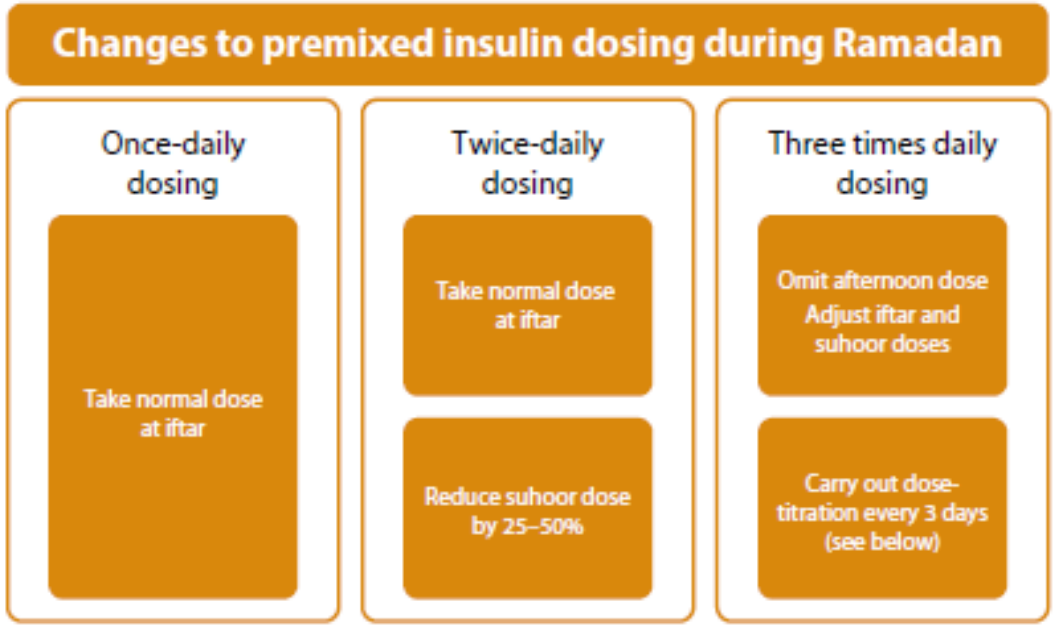
Diabetic medications

- **Insulin**


Changes to premixed insulin dosing during Ramadan
Once-daily dosing
Take normal dose at iftar
Twice-daily dosing
Take normal dose at iftar
Reduce suhoor dose by 25–50%
Three times daily dosing
Omit afternoon dose Adjust iftar and suhoor doses
Carry out dose-titration every 3 days (see below)

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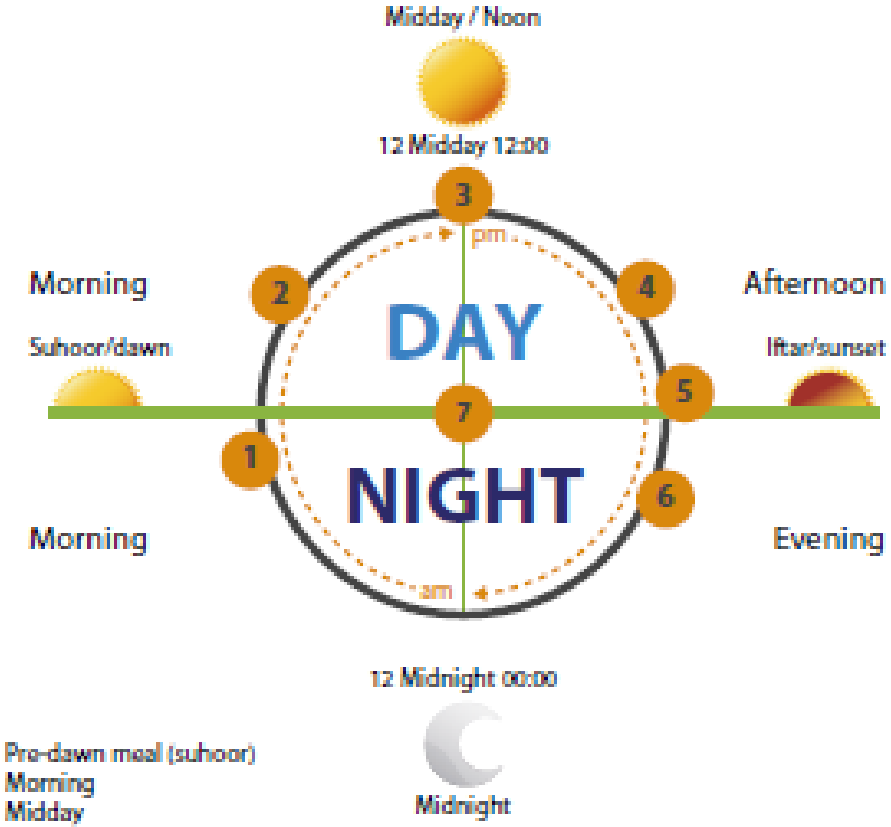
Diabetic medications

- **Checking RBS**



1. Pre-dawn meal (suhoor)
2. Morning
3. Midday
4. Mid-afternoon
5. Pre-sunset meal (iftar)
6. 2-hours after iftar
7. At any time when there are symptoms of hypoglycaemia/hyperglycaemia or feeling unwell

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Diabetic medications

- Adjusting bolus insulin doses during Ramadan

Pre-Sunset, Pre-Dawn Blood Glucose	Rapid- or Short-Acting Insulin Dose Adjustment
>250 mg/dL	Increase dose by 20%
>180 mg/dL	Increase dose by 10%
100–180 mg/dL	No change
<100 mg/dL or symptoms of hypoglycemia	Reduce dose by 10%
<70 mg/dL	Reduce dose by 20% and preferably avoid fast

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Home Messages

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Patients with chronic diseases

- **Patients who:**

1. Have chronic illnesses
2. Take medications on a regular basis

- Before Ramadan starts

- **They need to see their healthcare provider (Why??)**

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Patients with chronic diseases

1. To ensure their **ability** to fast
2. To adjust their **medications dosages** if necessary
3. To change **frequency of medications** to accommodate fasting schedule
4. For **close monitoring** of their health condition throughout the month Ramadan

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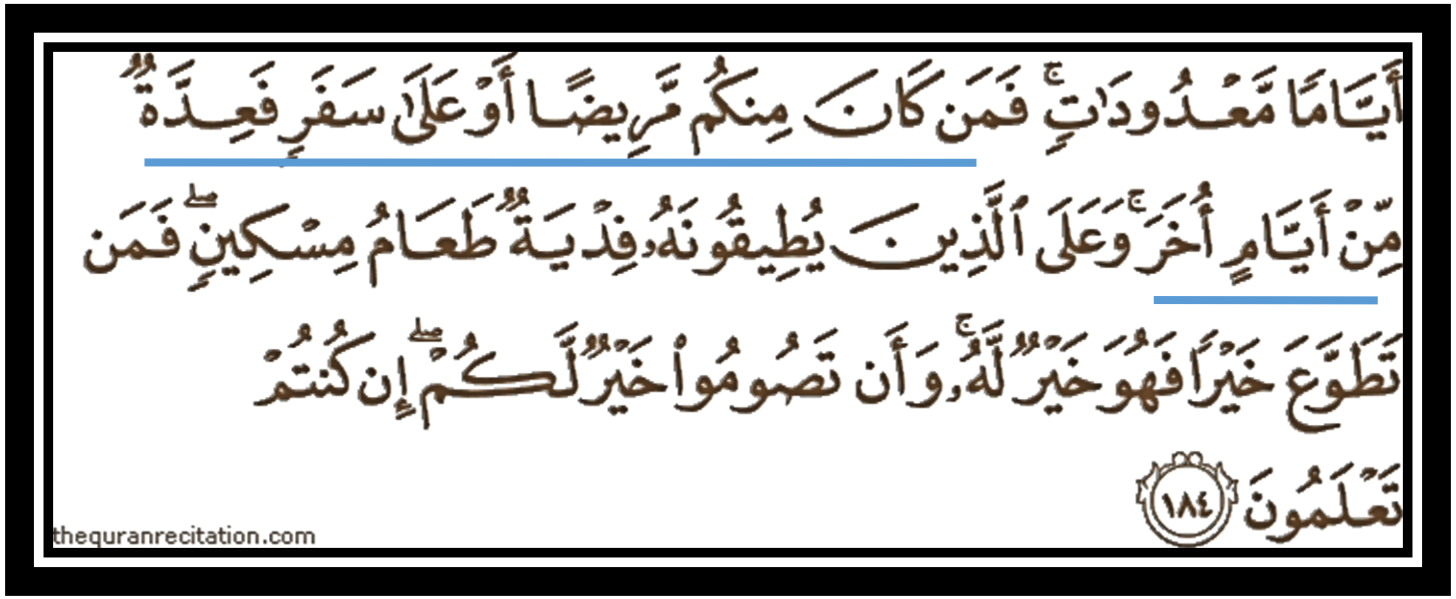
Patients with chronic diseases

- In case of the fasting will HARM patient health, patient can BREAKING the fast



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Routes and Fasting

- **Breaking the fasting:**
  - **Oral medication**
  - **Nutritional dosage forms**

- **Better to avoid during fasting:**
  - **Nasal drops and sprays**

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Routes and Fasting

- **Not Breaking the Fasting**
  - **Eye and ear drops**
  - **Sublingual tablets**
  - **Mouthwash, gargle, or oral spray**
  - **Creams, ointments, and medicated plasters**
  - **Vagina of pessaries, and vaginal washes**
  - **Injectable medication**
  - **Oxygen and anaesthetic gases**
  - **Inhalers**
  - **Anal injections or suppositories**

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Routes and Fasting

Delay the medication to after fasting time (better)

To ASK Islamic scholar

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Islam is Easy

شَهْرُ رَمَضَانَ ٱلَّذِىٓ أُنزِلَ فِيهِ ٱلْقُرْءَانُ هُدًى لِّلنَّاسِ
وَبَيِّنَٰتٍ مِّنَ ٱلْهُدَىٰ وَٱلْفُرْقَانِ ۚ فَمَن شَهِدَ مِنكُمُ ٱلشَّهْرَ
فَلْيَصُمْهُ ۖ وَمَن كَانَ مَرِيضًا أَوْ عَلَىٰ سَفَرٍ فَعِدَّةٌ مِّنْ
أَيَّامٍ أُخَرَ ۗ يُرِيدُ ٱللَّهُ بِكُمُ ٱلْيُسْرَ وَلَا يُرِيدُ بِكُمُ
ٱلْعُسْرَ وَلِتُكْمِلُوا۟ ٱلْعِدَّةَ وَلِتُكَبِّرُوا۟ ٱللَّهَ عَلَىٰ مَا
هَدَىٰكُمْ وَلَعَلَّكُمْ تَشْكُرُونَ ﴿١٨٥﴾

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Earn high reward

No Eating Or Drinking Whilst Fasting
Lower Your Gaze
No Arguing Or Fighting & Avoid Sins
No Swearing, Lying & Backbiting
No Smoking Try Quitting For Good
Don't Waste Time On Useless Activities
Do Not listen To Music
Pray All Your 5 Daily Salaah's On Time
Study & Learn Islamic Knowledge
Recite & Learn The Holy Qur'aan
Do Lots Of Dhikr
Make Lots Of Duaa
Give In Charity & Help The Poor
EARN HIGH REWARD WITH THE
RAMADHAAN
HIGH-WAY CODE

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